REMARKS

Pursuant to the Office Action dated September 12, 2006, all pending claims, namely claims 1-7, 10-22, 33, 34, 45 and 48-63, stand rejected. Applicants have made no amendments to the claims as it is believed that all claims are patentable as presented.

In the office action, the Examiner has requested that Applicants point out which claims, if any, recite subject matter that was not commonly owed at the time of the invention. Please note that all inventions defined in the claims were commonly owned at the time they were made.

Anticipation in view of Hagiwara et. al. (US 4,775,585 – "Hagiwara")

Claims 1-4, 10-12, 22, 33, 34, 48 and 49 stand rejected under 35 USC 102(b) as being anticipated by Hagiwara. It is alleged that Hagiwara teaches a polymer article having antibacterial properties as well as a physical properties similar to those of the polymer itself which contain antimicrobial zeolite particles and wherein the polymer can be highly hydrophilic. It is stated that the particle size of the zeolite can be selected depending upon the application and may be in the range of a few microns to tens of microns or even above several hundred microns. It is also noted that Hagiwara teaches the preparation of fiber or yarns of the antimicrobial polymer which inherently have an aspect ratio of greater than 2 and which may "be mix spun, mix woven, cross woven or union knitted with fibers or yarns having no metal-zeolite to give an antibacterial fiber article...." (Col. 10, lines 11-16). Finally, it is also alleged that the polyurethane of Hagiwara inherently possesses a water absorption at equilibrium of at least about 20% by weight.

Applicants respectfully traverse the rejection and request reconsideration. A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference" *Verdegall Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed, Circ. 1987). "The identical invention must be shown in as complete detail as is contained in the...claims." *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920

(Fed. Cir. 1989). Contrary to the assertion of the Patent Office, no such findings are present in Hagiwara.

Hagiwara is directed to antimicrobial polymer articles prepared from antimicrobial polymer compositions containing antimicrobial zeolites as the antimicrobial agent, which articles may be of any of a variety of **molded** shapes and dimensions including "granules, films, fibers, various types of containers, pipes and any other moulded articles." (Col. 9, lines 49-54). Nowhere is there any suggestion of microparticles of the polymer having dispersed therein even smaller particles of the antimicrobial agent or any reference to "molded articles" in the micron size range. In the examples, Hagiwara speaks of spinning fibers or forming staples from which the fibers are spun: both of which, as noted, would be expected to have aspect ratios above 2; however, the fibers are identified as long continuous filaments/yarns and the staples, from which the latter may be spun, have a length of 51mm. And while Hagiwara discloses that the antimicrobial fibers may be combined with non-antimicrobial fibers, this is completely different from and non-enabling of a polymer composition comprising a polymer matrix and dispersed therein discrete particles of a second polymer, the latter having dispersed therein an antimicrobial agent. Further, but for the one reference to the use of "a relatively highly hydrophilic polymer" at Col. 8, lines 14-18, no other mention is made of hydrophilic materials, nor is any mention made whatsoever to water absorption at equilibrium of any polymer, let alone a polyurethane. Indeed, though Hagiwara includes polyurethane in a long list of suitable polymers, it never actually prepares an antimicrobial polyurethane composition or article.

In contrast, the broadest claims of the present application specifically recite A) polymer particles suitable for use as an antimicrobial additive, the polymer particles i) having a high aspect ratio, greater than 2, whose largest dimension is from about 50 to about 500 microns, ii) having dispersed or incorporated therein a plurality of particles of an inorganic antimicrobial agent, and iii) being composed of a hydrophilic polymer having a water absorption at equilibrium of at least 5 weight percent, and B) a method of making the same. Neither the particle size limitations nor the specific use of a hydrophilic polymer, and certainly not one of the required degrees of hydrophilicity, are specifically taught or inherently described in Hagiwara. Furthermore,

nowhere does Hagiwara suggest or teach the formation of high aspect ratio, microparticles of the therein disclosed compositions or the use thereof as an additive for polymer matrix resins. As noted above, the smallest molded article shown or described by Hagiwara is the 51mm fiber staples, the smallest article altogether is the 20mm discs cut from the molded article for purposes of evaluating bactericidal activity (the latter, however, have a 1:1 aspect ratio). On the other hand, as noted, the largest dimension allowed by Applicants microparticles is 500 microns, a mere 1/100th that of the staple and 1/40th that of the cut disc of Hagiwara.

In light of Hagiwara's failure to expressly or inherently teaching each of the elements and claim limitations of the present invention, it is clear that no anticipation is found. Therefore the anticipation rejection of claims 1-4, 10-12, 22, 33, 34, 48 and 49 should be withdrawn.

Obviousness in over Hagiwara et. al. (US 4,775,585 – "Hagiwara") in view of Trogolo et. al. (US 6,436,422 – "Trogolo"), Gibson et. al. (US 6,413,536 – "Gibson") and further in view of Michal et. al. (US 6,287,285 – "Michal")

Claims 1-7, 10-22, 33, 34, 45 and 48-63 stand rejected under 35 USC 103(a) as being unpatentable over Hagiwara in view of Trogolo, Gibson, and further in view of Michal.

According to the Examiner, "Hagiwara could make a high aspect ratio antibacterial composition made of hydrophilic polymer and zeolite particles." Hagiwara is said to be deficient in disclosing the ceramic carrier, the ratio of hydrophilic polymer, the inorganic discoloration inhibiting agent and the sodium nitrate dopant.

Trogolo is cited as teaching the ion-exchange type antimicrobial zeolites and the use thereof in hydrophilic polymers for forming coatings wherein solids content of the coatings comprises from about 10 to about 99.99% by weight of hydrophilic polymer and from about 0.01 to 90 % by weight of the antimicrobial agent and of the controlled release of the antimicrobial ions in a range of from about 5 to 50 ppb. Trogolo is acknowledged as not "disclosing immersing the particles in a different polymer to alter the release."

Gibson is cited as providing a general teaching of biodegradable and non-biodegradable polymer additives for pharmaceutical compositions wherein the polymer additives are used to alter the release profile, add integrity to the composition or modify the properties of the composition. It is also alleged that suitable non-erodable polymer additives include polyurethanes.

According to the Examiner, it would have been obvious to one of ordinary skill in the art to use the teaching of Gibson by adding the high aspect ratio particles of both Hagiwara and Trogolo into a polymer to alter the release properties of the particles.

It is further acknowledged that neither Hagiwara or Trogolo disclose the use of a dopant, specifically sodium nitrate; however, it is alleged that Michal discloses the use of nitric oxide donor drugs, including sodium nitrate in hydrophilic coatings.

According to the Examiner, absent unexpected results, it would have been obvious

> "to modify the composition of Trogolo by adding a dopant, specifically sodium nitrate, as taught by Michal because of the expectation of relaxing smooth muscles of a vessel prior to, during and/or after angioplasty or stent replacement. Both Trogolo and Michal teach medical devices, specifically medical devices coated with a hydrophilic polymer. Therefore, it would have been obvious to add sodium nitrate to the composition of Hagiwara for the added benefits taught by Michal. The expected result would be a high aspect ratio antimicrobial composition comprising a hydrophilic polymer, an antimicrobial agent and a discoloring agent and a dopant."

Applicants respectfully traverse the rejections and request reconsideration. For convenience and clarity, Applicants will address the rejection in three parts corresponding to arguments/findings set forth in the rejection itself. The first assumption to be addressed will be the conclusion that Hagiwara and Trogolo, alone or together, teach high aspect ratio hydrophilic particles having an antimicrobial agent therein. The second is the alleged teaching, inference, or motivation of Gibson to add the aforementioned high aspect ratio particles to a polymer to alter the release characteristics of the antimicrobial agent. And, the third is the addition of the nitric oxide donor, specifically sodium nitrate, to achieve the benefits of Michal.

Hagiwara in view of Trogolo

It is well established that a *prima facie* case of obviousness requires a showing of some suggestion or motivation to modify the reference and/or combine the reference teachings, a showing of a reasonable expectation of success in doing so, and the reference(s) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. In re Vaeck 20 USPQ2d 1438 (Fed. Cir. 1991). The mere fact that the references can be combined or modified does not render the resultant combination obvious unless the prior art also suggest the desriability of the combination. In re Mills 16 USPQ2d 1430 (Fed. Cir. 1990) (See generally MPEP 2142 and 2143).

As noted above, Hagiwara fails to teach that which it is alleged. First, as Hagiwara specifically states, it is directed to molded articles of an antimicrobial composition. These molded articles may be in the shape of "granules, films, fibers, various types of containers, pipes and any other moulded articles" of varying dimensions (Col. 9, lines 49-54). Nothing in Hagiwara teaches, suggests or infers microparticles of its compositions, let alone of an antimicrobial hydrophilic composition, nor is it even clear how one might "mold" such microparticles. Furthermore, there is no teaching, inference, or suggestion that such microparticles, if formed, could be used as and in substitution for the antimicrobial agents described therein. As set forth in great detail in Applicants' last response, these microparticle additives are used as the antimicrobial agent for incorporation into polymer compositions, like those of Hagiwara, for providing enhanced antimicrobial performance as compared to the neat antimicrobial active agent itself.

Additionally, despite the Examiner's assertion that "because Hagiwara uses polyurethane in an antimicrobial composition, it is inherently having a water absorption at equilibrium of at least 20% by weight," Hagiwara never exemplifies a polyurethane and, further, makes no mention of the degree of hydrophilicity. Indeed, the only reference to hydrophilic properties in all of Hagiwara is the one ancillary comment as to the antimicrobial performance when used in a "relatively highly hydrophilic polymer." As set forth in MPEP 2144.03(A), **"Official notice**

unsupported by documentary evidence should only be taken by the examiner where the facts asserted to be well-know, or to be common knowledge in the art, are capable of instant and unquestionable demonstration as being well-known." The assertion that Hagiwara uses a hydrophilic polyurethane, let alone one having water absorption at equilibrium of at least 20 weight percent, is completely false and without foundation or support.

Finally, the Examiner's statement that "Hagiwara **could** make a high aspect ratio antibacterial composition made of a hydrophilic polymer and zeolite particles" (emphasis added), is not the basis upon which prima facie obviousness is founded. **Whether something could be made is not the question, the question is whether the reference teaches, suggests or motivates one to make that which it is alleged to make:** here it does not. Using the Examiner's reasoning, in hindsight, Hagiwara **could** also make a coated article as taught by Trogolo, yet it is clear that Trogolo was patentable over Hagiwara as it was cited in the examination of Trogolo. Furthermore, Hagiwara could make any number of articles that are the subject of dozens, if not hundreds, of patents following Hagiwara; yet, again, these too were deemed patentable. Again, clearly, it is not a matter of "could" but what it taught or motivated.

Further reliance upon Trogolo does not help establish prima facie obviousness. First, Hagiwara is directed to antimicrobial molded articles whereas Trogolo is directed to antimicrobial coating compostions for treating and, hence, imparting antimicrobial properties to articles and substrates. The former involves incorporating the antimicrobial agent into a polymer melt. The latter involves dissolving the polymer in a suitable solvent that has suspended therein the antimicrobial agent or combining two solutions, one having the dissolved polymer and the other having the suspended antimicrobial agent, and using the resultant solutions as a coating material, which, upon evaporation of the solvent, leaves an antimicrobial hydrophilic polymer film on the treated article or substrate. As stated at MPEP 2143.02(VI), "[I]f the proposed modification or combination of the prior art would change the principal of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. In re Ratti, 123 USPQ 349 (CCPA 1959)." One skilled in the art of coatings would not look to molding compositions for coatings nor would one skilled in the art of molded

articles look to coatings for new molding compositions. Thus, the references are not combinable and, therefore, the Examiner has not established a case of prima facie obviousness.

Furthermore, even if the Hagiwara and Trogolo were combinable, the best that the combined teachings would provide is, generally, hydrophilic molding compositions. Despite the Examiner's conclusion that both teach polymer particles of a hydrophilic polymer having incorporated therein an antimicrobial zeolite, nowhere does Trogolo speak of particles of a hydrophilic polymer with the antimicrobial zeolite and, as noted above, Hagiwara only suggests, as one of many shapes, granules. Nothing suggests i) microparticles as claimed, especially ones having an aspect ratio of greater than 2 and a maximum dimension of 500 microns and ii) the use of a hydrophilic polymer having a water absorption at equilibrium of at last 5 weight percent. Nor is there any motivation in either reference or the combined teachings to prepare such microparticles. Since Trogolo prepares coatings, they only teach liquid materials that, upon evaporation of the solvent, form polymer films on a substrate, not particles. As previously stated, Hagiwara forms molded articles from a melt blend of the polymer and the antimicrobial agent. Even if one could mold a 500 micron particle, there is no motivation to do so. The molding industry tries to avoid powders, which a 500 micron particle compositon would be, due to the difficulty of handling those materials. Regardless, as noted above, the second step of building a case of obviousness requires the disclosure of all the required elements and limitations being claimed. No such finding is present in either or both references.

Applicants acknowledge the teaching of Trogolo with respect to the compositional make-up of the coatings as well as the release rate of the antimicrobial active; however, again, this is relative to a coating: a homogeneous film of the antimicrobial polymer, not particles, and certainly not microparticles. Furthermore, while Trogolo may suggest that the individual particles may release, there in no teaching or expectation of how that release may be effected when the individual particles are subsequently incorporated into another polymer. As noted elsewhere, the high aspect ratio antimicrobial additives of the present invention are useful as and are intended for use as substitutes for the neat antimicrobial agent of Trogolo and Hagiwara. Neither reference teaches, suggests, infers the option or desirability of using the antimicrobial

hydrophilic polymer microparticles of the present invention in substitution for the neat inorganic antimicrobial agents used in each, let alone provides any expectation or prediction that such use will result in polymers, molded articles and coatings having enhanced antimicrobial performance, especially improved longevity and release control, regardless of the polymer into which they are added.

Hagiwara in view of Trogolo and Gibson

In effort to address this acknowledged shortcoming of Trogolo and Hagiwara, the Examiner points to Gibson as motivation to add the antimicrobial microparticles to another polymer for altering the release rate of the antimicrobial active. Gibson, however, is directed to non-polymeric compounds and compositions that form liquid high viscosity materials for, amongst other applications, delivery of bioligically active substances in a controlled fashion. These compositions may further include minor amounts, up to 20 wt %, preferably "1, 2, or 5 percent to about 10 by weight" of a biodegradable or non-biodegradable polymer additive (Col. 15, lines 32-40). According to the Examiner, one of the suitable polymer additives is polyurethane. In following the Examiner states that, "[I]t would have been obvious to one of ordinary skill in the art to use the teaching of Gibson by adding the high aspect ratio particles of both Hagiwara and Trogolo into a polymer to alter the release properties of the particles."

First, it is believed that Gibson is truly non-analogous art. As set forth in MPEP 2141.01(a), "[I]n order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the filed of the applicant's endeavor or, if not, then be reasonably pertinent to the paricular problem with which the inventor was concerned." Such a finding is not present here. Gibson is concerned with liquid, high viscosity materials suitable as carriers and delivery means for bio-active substances. These materials are applied either as a topical paste, salve, or the like or as an implant or injected material to a living organism, e.g., a patient, animal, plant, etc., to effect delivery by release of a therein contained bio-active agent to the treated tissue. These nonpolymeric liquids may also contain minor amounts of certain polymer materials; yet, the compositions of Gibson are nevertheless liquid, non-polymeric, non-

solidifying treatments. Such materials are of interest to doctors, veterinarians, horticulturalists, etc., but certainly of no interest or import to a molding or coating specialist. Furthermore, as noted, Gibson adds its bioactive agent to a liquid, and specifically requires a liquid; whereas Applicant's add their antimicrobial agent to a solid and requires a solid. Gibson is directed to treatment of a living organism whereas Applicants are focused on preventing the growth of microorganisms on a substrate or article. Thus, not only are the fields of endeavor unrelated, but the very objectives are as well.

Furthermore, even if the Patent Office were to maintain Gibson as being anologous art, prima facie obviousness is not found as the combination of Gibson with the art is neither appropriate not possible. As noted above, Gibson teaches the combination of the liquid carrier and, dispersed therein, a bioactive agent and a polymer additive and tells us that the addition of the polymer additive affects the properties and characteristics of the liquid in several ways, one of which relates to the release of the bioactive agent. Both Hagiwara and Trogolo teach adding a solid antimicrobial agent to a solid polymer (or to the solution of the polymer in the case of the uncured coating) to impart antimicrobial characteristics to the solid polymer. Applicants are having a difficult time trying to ascertain how the combination proposed by the Examiner is to be effected: what elements are being combined and in what way? Setting aside the fact that Hagiwara and Trogolo do not teach what the Examiner asserts they do, are we to presume that instead of Gibson's addition of the bioactive agent and the polymer additive, the Examiner is theorizing the bioactive agent first be combined with the polymer additive and that added as a single ingredient to the non-polymeric liquid carrier? If so, upon what basis is the Examiner asserting that such an alternative method and composition will perform as intended by Gibson? As noted, Gibson seems to assert that the polymer additive has an influence on the liquid carrier which changes the release characteristics of the bioactive from that liquid carrier. Nothing, however, suggests or infers what might happen if the bioactive were in the polymer additive. There one would need to be concerned with the transfer from the polymer additive to the liquid carrier and then from the liquid carrier to the target tissue.

Regardless, relative to the use of Applicants high aspect ratio, antimicrobial hydrophilic polymer additive microparticles in a solid polymer matrix, Gibson can not and does not provide any degree of predicability or expectation of antimicrobial performance, especially not the enehanced antimicrobial performance found. Liquid and solid systems are two complete different universes. If and how something migrates and releases from one is not translatable to the other. Thus, prima facie obviousness is not found.

Hagiwara in view of Trogolo, Gibson and Michal

Finally, the further reliance upon Michal relative to the addition of the dopant is moot in light of the patentability of the independent claim. Nevertheless, it should be pointed out that the rejection applies a hindsight reasoning in its attempt to reconstruct Applicants' invention by specifically assuming that the ultimate end-use application is a specific type of medical device where insertion and lubricity is an issue out of the myriad of potential applications for Applicants' invention. In the absence of that very specific and unique set of circumstances put forth by the Examiner, the chance probability of all the claimed elements being used in a common application, is minimal. Furthermore, even if one accepts the chance circumstance, there is no expectation that the alleged obvious combination would provide the results attained.

It is well established in Patent Law that "[O]bviousness cannot be predicated on what is not known at the time the invention is made, even if the inherency of a certain feature is later established. *In re Rijckaert* 28 USPQ2d 1955 (Fed. Cir. 1993).

Putting aside the very elements and benefits of the present invention, Trogolo teaches one to expect antimicrobial efficacy by coating a medical device with a hydrophilic polymer having incorporated therein an antimicrobial agent. Michal teaches that one can improve the ease with which a medical device is inserted into a vessel or tissue by using a medical device that has been coated with a coating having a hydrophilic additive. Independently, it also teaches that one may use certain therapeutic agents, including nitric oxide donors, such as sodium nitrate, as a coating additive to act as a vasodilator in coatings to be applied to medical devices, such as stents,

catheters and the like, to relax the smooth muscles of a vessel, again to aid in the insertion of the device. Consistent with Michal's repeated use of "therapeutic, diagnostic or hydrophilic agent," nothing suggests, infers or motivates one to use both the hydrophilic agent and the nitric oxide donor therapeutic agent in the coating, let alone to select sodium nitrate as the nitric oxide donor. However, even if one beat the odds and came to that specific combination, there is nothing that would suggest that by doing so, in the unique circumstance that the coating also contained an ion-exchange type antimicrobial agent, the sodium nitrate would also serve as a dopant for the antimicrobial agent. Furthermore, there is nothing to suggest what effect, if any, the 'inherent' secondary role would have on the primary role, i.e., as a vasodilator, of the sodium nitrate.

Since none of the art actually made the theorized combination of neat antimicrobial agent, hydrophilic polymer and nitric oxide donor, more specifically sodium nitrate, let alone the high aspect ratio, hydrophilic polymer antimicrobial additive particles as claimed, the result of the combination, which is not predicted by what was taught by the references, could not be foreseen or nor was it inherent. Thus, again, no case of prima facie obviousness has been established.

Claims Fees

Inasmuch as no changes have been made to the number of pending claims in the application, no additional claims fees are owed

Supplemental IDS

In continuing compliance with their Duty or Disclosure, Applicants submit for consideration the art listed on the attached Form PTO/SB/08A pursuant to 37 CFR 1.97(c). But for the Yashiki reference, the cited art first came to the attention of Applicants by way of the October 17, 2006 and October 26, 2006 Office Actions issued in co-pending related patent application serial Nos. 10/032,370 and 11/336,699, respectively. Yashiki was identified by the undersigned within the last month in an effort to identify a certain polyol identified therein. None of these references

have been cited in a communication from a foreign patent office in the prosecution of a foreign counterpart application nor were they known to Applicants for more than three months prior to the date of this filing. Finally, US 6,399,735 is the US equivalent to the Henkel International Patent Publication, and, therefore, a copy of the latter is not enclosed. No fee is required.

Conclusion

In light of the foregoing remarks, Applicants reaffirm their belief that the claims as presented are clearly patentable over the art. The Examiner is requested to also review the prior response which concisely sets forth a detailed explanation of the various elements and embodiments of the claimed invention. Despite the many allegations and conclusions of the Examiner, Applicants have fully rebutted the arguments presented. None of the art, alone or in combination specifically teaches, suggests or motivates one to prepare the narrowly defined high aspect ratio microparticles claimed or provides any inference or suggestion that those particles could be used as a polymer additive for imparting improved antimicrobial performance to a polymer matrix as compared a similar polymer matrix where the same amount, if not a lesser amount, of antimicrobial agent is added in its neat form. Thus, Applicants respectfully request that the rejections be withdrawn and the application be passed on to allowance.

Respectfully submitted,

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